Journal of Human Hypertension (1996) 10, 349–352

Are four duplicate remeasurements sufficient for diagnosing mild hypertension?

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The aim of this study was to investigate if four duplicate blood pressure (BP) remeasurements are sufficient for diagnosing hypertension in potentially hypertensive subjects. The subjects were 99 outpatients who were included on the basis of elevated diastolic (95 ≤ DBP ≤ 115 mm Hg) or systolic (160 ≤ SBP ≤ 200 mm Hg) BP. After inclusion all patients underwent nine subsequent duplicate BP measurements over a period of 7 months.

None of the patients received hypotensive drug treatment during the study. Between the first (initial) and second measurements there were significant reductions in systolic (161.0–152.5 mm Hg) and diastolic (101.5–97.1 mm Hg) BPs ($P < 0.01$). Differences between the subsequent measurements were not statistically significant. A linear regression analysis proved that the 'conceptual average BP' (the average of the last five visits) which was chosen as the reference value was stable. The decline of standard deviations of differences between two, three and four duplicate remeasurements on one hand, and the reference value on the other was found to be strikingly small. After four duplicate remeasurements, there was misclassification in 56% (systolic) and 38% (diastolic). We conclude that the numbers of two, three or four BP measurements recommended by international guidelines for diagnosing hypertension are too low. Even after four duplicate remeasurements a considerable amount of misclassification remains.

Keywords: diagnosis; blood pressure measurement; blood pressure determination

Introduction

Given the enormous within-person variability of blood pressure (BP), the phenomenon of 'white-coat hypertension' and measurement errors, one might wonder whether the few repeated measurements recommended in guidelines are enough for diagnosing hypertension. The Fifth Report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure states that initial elevated readings should be confirmed on at least two subsequent occasions over a period of one to several weeks.[1] The management guidelines of the British Hypertension Society recommend two or more BP measurements in the sitting position on each visit on up to four separate occasions.[2] The 'NHG-Standard Hypertension', a guideline published by the Dutch College of General Practitioners, proposes at least five duplicate remeasurements in patients with diastolic initial BPs between 95 and 105 mm Hg.[3]

In two studies in patients diagnosed as mild hypertensives, one third to one half of all those taking placebo were later found to have diastolic pressures below 90 mm Hg.[4,5] This raises the question of the correctness of the initial diagnosis.

In the 1940s, Smirk and co-workers investigated the differences between BP measured in the doctor's office (casual BP) and BP measured under highly standardised conditions after a period of rest (basal BP).[6–9] However, there are two problems with the concept of basal BP: (1) it is almost impossible to measure in general and clinical practice; (2) the prognostic value and clinical relevance remain unclear.

The objective of the present study is to answer the question if four duplicate remeasurements are sufficient for diagnosing hypertension in potentially mildly to moderately hypertensive outpatients? In other words is, in these patients, the average of four duplicate remeasurements a solid basis to start a probably lifelong, drug treatment? This question is relevant since the importance of a correct diagnosis and classification is in the subsequent treatment. Misclassification may result in unjustified treatment, or in an incorrect withholding of treatment. This dilemma is particularly experienced in general practice, where the majority of hypertensive patients are diagnosed, and where most hypertensives have BP values around the threshold level for treatment.

Patients and methods

The study was approved by the ethical review committee of the University Hospital of Maastricht, The

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Received 28 March 1995; revised 1 February 1996; accepted 15 April 1996

Netherlands. All subjects gave written informed consent for participation in the study.

Seventeen general practitioners participated in the study. All of them were given instructions on the correct technique of measuring BP.[10] Phase V of Korotkoff tones was recorded as the level of diastolic blood pressure (DBP). Patients were selected on the basis of an elevated initial BP.

Inclusion criteria:

- mean of two systolic values measured in one visit between 160 and 200 mm Hg or mean of two diastolic measurements between 95 and 115 mm Hg;
- age between 20 and 75 years.

Exclusion criteria:

- known hypertension or hypotensive treatment in the year preceding the intended inclusion;
- secondary hypertension;
- congestive heart failure or unstable angina;
- pregnancy.

After inclusion (V1), nine visits (V2, V3, ... V10) were arranged over the next 7 months. At each visit, the BP was measured twice. V2, V3 and V4 took place during the 4 weeks following V1, while V5, V6, V7, V8, V9 and V10 were made over the subsequent period of 6 months.

BP was measured by the general practitioner in his office using a conventional calibrated mercury sphygmomanometer, provided with a standard-sized cuff (12 × 35 cm).

Analysis

Results were reported as systolic and diastolic means, standard errors of the mean and standard deviations of all patients at V1, V2, ... V10. Differences between the means of two successive readings (V1 *vs* V2; V2 *vs* V3, . . .) were analysed using Student's paired *t*-test. The average systolic blood pressure (SBP) and DBP of V6, V7, V8, V9 and V10 (10 BP measurements) over the last 5 months of the study were regarded as the 'conceptual average BP' (CABP). This reference value is a compromise between the mean value of eight measurements in four visits used by Armitage *et al*[11] and the mean of 12 measurements in six visits used by Watson *et al*.[12]

A linear regression analysis was done to provide a basis for the CABP. Therefore, the slope of V6, V7, V8, V9 and V10 was calculated for each participating subject. A Student's paired *t*-test between the mean slope and zero was used to assess the stability of the CABP. Mean differences and standard deviations of the differences (SDD) were calculated between CABP and V2/V3, CABP and V2/V3/V4, CABP and V3/V4/V5 and CABP and V2/V3/V4/V5.[13].

Finally, the percentages of misclassification were calculated on the basis of one (V2); two (V2/V3), three (V2/V3/V4) and four (V2/V3/V4/V5) duplicate remeasurements. Misclassification was defined as 5 mm Hg or more difference between the initial remeasurements and the CABP, using the same definition as Watson *et al*.[12]

Results

One hundred and fourteen patients were included in the study of which 15 dropped out (10 men and 5 women; mean systolic V1 164.7 mm Hg, mean diastolic V1 105.1 mm Hg): 6 patients started antihypertensive drug treatment, one patient had a heart attack and the other eight withdrew for personal, non-medical reasons.

Ninety-nine patients completed the study, 49 men and 50 women (mean age 48 years). Mean systolic V1 was 161.0 mm Hg and mean diastolic V1 101.5 mm Hg. The dropouts had higher average BPs when entering the study. Systolic and diastolic means, standard errors (s.e.) and standard deviations are given in Table 1. There were significant differences between systolic V1 and V2 (8.5 mm Hg, $P < 0.001$) and between diastolic V1 and V2 (4.5 mm Hg, $P < 0.001$). Differences between the mean values of the other pairs of successive measurements (V2 *vs* V3; V3 *vs* V4, . . .) were not statistically significant (Table 1).

The mean slope of systolic CABP was −0.04 (s.e. of mean 0.4), that of diastolic CABP −0.11 (s.e. of mean 0.2). Student's paired *t*-test showed no significant differences between these mean slopes and zero ($P = 0.9$ resp $P = 0.6$). This indicates that our conceptual average BP can be regarded as a stable reference value. There is a minor decline in mean differences and SDDs (SBP from 11.4–9.6 mm Hg; DBP from 6.4–5.3 mm Hg) of systolic and diastolic CABP *vs* V2/V3, CABP *vs* V2/V3/V4, CABP and V3/V4/V5 and CABP *vs* V2/V3/V4/V5 (Table 2). The percentages of misclassification after one, two, three and four duplicate remeasurements show a decline. However, after four remeasurements there is still misclassification in 56% (SBP) and 38% (DBP) of the subjects (Table 3).

Discussion

A linear regression analysis proved that the 'conceptual average BP' which was chosen as the reference value was stable. It was found that there was a statistically significant fall in systolic and diastolic BP between the first and second measurements. This can be regarded as a consequence of the selection process. It reflects the well known 'regression towards the mean' phenomenon, in addition to the causes mentioned in the introductionary part. Using analyses of variance, Dunne[14] also found a highly significant difference between the first and second occasion, in contrast to the minor differences between subsequent occasions. After the second measurement there was a slight fall in mean DBP, without significant differences between two successive readings. After the second measurement, mean SBP seemed to oscillate around a mean value. The decline of the standard deviations of the differences between two, three and four duplicate remeasurements on the one hand and the reference value CABP on the other was found to be strikingly small. Excluding not only the first, but also the second measurement resulted in the best, though still disappointing agreement with the CABP. After four dupli-

Table 1 Means, standard errors and standard deviations, of systolic and diastolic blood pressures at V1, V2, ... V10, and *P*-values of the paired sample *t*-tests of successive readings

	Mean	*Standard error*	*Standard deviation*	*P-value*
Systolic blood pressure				
V1	161.0	1.8	17.4	0.00 (V1 *vs* V2)
V2	152.5	1.7	16.8	0.91 (V2 *vs* V3)
V3	152.8	1.8	17.3	0.24 (V3 *vs* V4)
V4	151.2	1.6	15.6	0.81 (V4 *vs* V5)
V5	151.5	1.7	16.4	0.40 (V5 *vs* V6)
V6	150.4	1.7	16.7	0.05 (V6 *vs* V7)
V7	153.4	1.9	18.9	0.21 (V7 *vs* V8)
V8	150.8	1.7	16.9	0.88 (V8 *vs* V9)
V9	151.7	1.8	17.3	0.64 (V9 *vs* V10)
V10	150.7	1.8	17.0	
Diastolic blood pressure				
V1	101.4	0.6	5.6	0.00 (V1 *vs* V2)
V2	96.9	1.0	9.6	0.06 (V2 *vs* V3)
V3	95.5	0.9	8.9	0.79 (V3 *vs* V4)
V4	95.2	0.9	8.8	0.31 (V4 *vs* V5)
V5	94.3	1.0	9.7	0.55 (V5 *vs* V6)
V6	94.9	0.9	8.9	0.98 (V6 *vs* V7)
V7	94.8	1.0	9.7	0.89 (V7 *vs* V8)
V8	94.8	0.9	9.0	0.55 (V8 *vs* V9)
V9	94.4	0.9	9.3	0.95 (V9 *vs* V10)
V10	93.7	1.1	9.9	

Vx: average of duplicate measurements on visit x.

Table 2 Mean differences (mean), standard errors (s.e.) and standard deviations of mean differences (SDD) between conceptual average blood pressure and V2/3, V2/3/4, V3/4/5 and V2/3/4/5

	Systolic blood pressure			*Diastolic blood pressure*		
	mean	*s.e.*	*SDD*	*mean*	*s.e.*	*SDD*
V2/3	1.1	1.1	11.4	−1.6	0.6	6.4
V2/3/4	0.6	1.0	10.3	−1.2	0.6	5.8
V3/4/5	0.3	1.0	10.0	0.3	0.6	5.5
V2/3/4/5	0.5	1.0	9.6	0.8	0.5	5.3

Table 3 Proportion of misclassification, defined as a difference of 5 mm Hg or more between CABP and V2/3, V2/3/4, V2/3/4/5 after two, three and four duplicate remeasurements

Systolic blood pressure			*Diastolic blood pressure*		
V2/3	V2/3/4	V2/3/4/5	V2/3	V2/3/4	V2/3/4/5
0.67	0.55	0.56	0.40	0.39	0.38

cate remeasurements, there was misclassification in 56% (systolic) and 38% of all patients. These results are even slightly worse than those found by Watson *et al*[13] in their study (50% misclassification after four remeasurements for SBP, 32% for DBP) This minor difference may have been caused by different inclusion criteria and different numbers of patients included. As we did not have more measurements, we could not calculate the misclassification after five and six remeasurements. Applying Cronbach's generalizability theory, Llabre[15] and co-workers demonstrated that for normotensive subjects at least six readings of systolic and 6 to 10 readings of DBP are needed.

We conclude that the numbers of two, three or four BP measurements recommended by international guidelines for diagnosing mild hypertension are too low.[1,2] Even after four duplicate remeasurements a considerable amount of misclassification remains.

Acknowledgement

The study was supported by a grant from the Netherlands Organisation for Scientific Research (NWO), Grant number 900.715.169.

References

1 Anonymous. The Fifth Report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure. *Arch Intern Med* 1993; **153**: 154–183.
2 Sever P *et al*. Management guidelines in essential hypertension: report of the second working party of the British Hypertension Society. *Br Med J* 1993; **306**: 983–987.
3 Van Binsbergen JJ *et al*. NHG-Standaard Hypertensie. *Huisarts Wet* 1991; **34** (8): 389–395.
4 Report of the Management Committee of the Australian Therapeutic Trial in Mild Hypertension. Untreated mild hypertension. *Lancet* 1982; i: 185– 91.
5 Medical Research Council Working Party. MRC trial of treatment of mild hypertension: principal results. *Br Med J* 1985; **291**: 97–104.
6 Alam GM, Smirk FH. Casual and basal blood pressures. I. In British and Egyptian men. *Br Heart J* 1943, **5**: 152–155.
7 Alam GM, Smirk FH. Causal and basal blood pressures. II. In essential hypertension. Br Heart J 1943; **5**: 156–160.
8 Gatman M, Amin M, Smirk FH. Casual and basal blood pressures. III. In renal hypertension. *Br Heart J* 1943; **5**: 161–162.

9 Smirk FH. Casual and basal blood pressures. IV. Their relationship to the supplemental pressure with a note on statistical implications. *Br Heart J* 1944; **6**: 174–182.
10 British Hypertension Society recommendations on blood pressure measurement. In: Birkenhaeger WH and Reid JL, (eds), *Handbook of Hypertension* Volume 14. Elsevier: Amsterdam, 1991, App I, pp. 387–395.
11 Armitage P, Fox W, Rose GA, Tinker CM. The variability of measurements of casual blood pressure. II. Survey experience. *Clin Sci* 1966; **30**: 337–344.
12 Watson RDS *et al.* Variation in cuff blood pressure in untreated outpatients with mild hypertension: implications for initiating antihypertensive treatment. *J Hypertens* 1987; **5**: 207–211.
13 Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986; **i**: 307–310.
14 Dunne JF. Variation of blood-pressure in untreated hypertensive outpatients. *Lancet* 1969; **i**: 391–392.
15 Llabre MM *et al.* How many blood pressure measurements are enough?: An application of generalizability theory to the study of blood pressure reliability. *Psychophysiology* 1988; **25**: 97–106.